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EDITORIAL · REDAKSIONEEL

VINBLASTINE

A NEW INTRAVENOUS ANTI-CANCER ALKALOID

A new anti-cancer agent from a plant source has been made available for the treatment of generalized Hodgkin's disease and choriocarcinoma.

The new drug (introduced under the trademark Velbe) is the sulphate salt of vinblastine (VLB), an alkaloid extracted from the periwinkle, a garden shrub. Although it is found in many gardens, the dried plant is obtained for processing in large quantities from the Far East.

The activity of periwinkle extracts against cancers in animals was discovered independently by scientists of the Collip Research Laboratories at the University of Western Ontario, London, Ontario, Canada, and of the Lilly Research Laboratories, Indianapolis, U.S.A.

Vinblastine has been studied in 300 patients with a variety of malignant diseases. It has been released in the United States by the Food and Drug Administration for the treatment of Hodgkin's disease and choriocarcinoma. The evaluation of results in other cancers has not been completed.

The clinical trial is being expanded, and now includes more than 200 investigators throughout Canada, Australia, the United States, Europe, South Africa and Latin America.

VINBLASTIEN

'N NUWE BINNE-AARSE ANTI-KANKER-ALKALOÏED

'n Nuwe anti-kankermiddel, verkry uit 'n plantaardige bron, is tans beskikbaar vir die behandeling van verspreide Hodgkin-siekte en choriokarsinoom.

Die nuwe middel (wat in die handel as Velbe bekend staan) is die sulfaatsout van vinblastien (VLB), 'n alkaloïed verkry van die maagdeblom (*periwinkle*), 'n tuinstruikgewas. Hoewel dit in baie tuine aangetref word, word groot hoeveelhede van die droë plant vir bewerkingsdoeleindes uit die Verre Ooste ingegevoer.

Die aktiwiteit van maagdeblom-uittreksel teen kankers by diere is onafhanklik ontdek deur wetenskaplikes by die Collip-navorsingslaboratorium aan die Universiteit van Wes-Ontario, Londen, Ontario, Kanada, en aan die Lilly-navorsingslaboratorium, Indianapolis, V.S.A.

'n Studie is gemaak van die effek van vinblastien op 300 pasiënte lydende aan 'n verskeidenheid van kwaadaardige kwale. In die Verenigde State word dit deur die Voedsel- en Geneesmiddeladministrasie aanbeveel vir die behandeling van Hodgkin se siekte en choriokarsinoom. Die evaluasie van die resultate wat met ander kankersoorte behaal is, is nog nie voltooi nie.

In the United States, for some 10,000 to 15,000 cases of Hodgkin's disease there are only 700 cases of choriocarcinoma. Together these 2 malignancies thus represent only a small percentage of all cancer cases.

The first clinical study of the drug was initiated in March 1959, at the Indiana University Medical Center, Indianapolis, U.S.A. Other investigations followed immediately at the Ontario Cancer Institute, Princess Margaret Hospital, Toronto, Canada; at the Lilly Laboratory for Clinical Research, Marion County General Hospital, Indianapolis, U.S.A.; and at the National Cancer Institute, Bethesda, Maryland, U.S.A.

Both the Lilly and the Canadian clinicians reported particularly good effects against Hodgkin's disease. It was at the National Cancer Institute that the drug's usefulness in choriocarcinoma was first noted.

Clinical studies of Hodgkin's disease may be summarized as follows:

1. Significant tumour shrinkage and improvement in general physical condition were obtained in 31 of 34 patients. Twenty-six of these had previously failed to respond to other available methods of treatment.
2. Not less than 75% reduction in tumour masses occurred in at least half of the 34 cases.
3. To date (March 1961) 23 patients placed on maintenance doses have kept their improvement without relapse.
4. Many patients benefited by the drug continue to be maintained in their improvement for periods ranging from several months to more than one year.
5. Several patients have lost, at least for the present, all evidence of Hodgkin's disease.

There is no evidence, however, that the drug in any instance has 'cured' Hodgkin's disease or any other form of human cancer.

At the National Cancer Institute, vinblastine had produced antitumour effects in 7 of 10 patients with choriocarcinoma which failed to respond to other drugs. Five patients obtained clinical remissions of the disease. Four of the remissions have lasted from several months to a year or more.

The further reports on this new anti-cancer drug will be awaited with great interest.

Die kliniese proefnemings is uitgebrei, en sluit tans meer as 200 navorsingswerkers in Kanada, Australië, die Verenigde State, Europa, Suid-Afrika en Latyns-Amerika in.

Vir iedere 10,000 tot 15,000 gevalle van Hodgkin se siekte in die Verenigde State is daar slegs 700 gevalle van choriokarsinoom. Saam verteenwoordig hierdie 2 kwaadaardige kwale dus net 'n klein persentasie van alle kankergevalle.

Die eerste kliniese bestudering van die middel is in Maart 1959 aan die Mediese Sentrum van die Indiana-universiteit, Indianapolis, V.S.A., van stapel gestuur. Verdere navorsingswerk het onmiddellik hierop gevolg aan die Ontario-kankerinstituut, Prinses Margaret-hospitaal, Toronto, Kanada; aan die Lilly-laboratorium vir Kliniese Navorsing, Algemene Hospitaal, Marion County, Indianapolis, V.S.A.; en aan die Nasionale Kankerinstituut, Bethesda, Maryland, V.S.A.

Sowel die Lilly- as die Kanadese kliniste rapporteer dat hulle 'n besonder goeie effek in gevalle van Hodgkin se siekte behaal het. Dit was by die Nasionale Kankerinstituut dat die middel se nuttigheid in gevalle van choriokarsinoom vir die eerste keer opgemerk is.

Die kliniese studie van Hodgkin se siekte kan soos volg saamgevat word:

1. Betekenisvolle gewas-krimping en verbetering van die algemene fisiese toestand is waargeneem by 31 uit 34 pasiënte. Ses-en-twintig van hulle het vroeër geen reaksie op ander beskikbare behandelingsmetodes getoon nie.
2. By ten minste die helfte van die 34 pasiënte is die tumormassas met nie minder as 75% verminder nie.
3. Tot op hede (Maart 1961) het 23 pasiënte wat met instandhoudingsdosisse behandel is, hul verbetering sonder relaps volgehou.
4. Baie pasiënte wat deur behandeling met die middel gebaat is, het hul verbetering volgehou oor tydperke wat van etlike maande tot meer as 'n jaar gewissel het.
5. By etlike pasiënte is daar op die oomblik altans geen bewys van Hodgkin se siekte nie.

Daar is egter geen bewys dat die middel in enige besondere geval Hodgkin se siekte, of enige ander vorm van kanker by die mens ‚genees' het nie.

By die Nasionale Kankerinstituut het vinblastien 'n anti-gewaseffek gehad op 7 uit 10 pasiënte met choriokarsinoom wat nie op ander middels gereageer het nie. By vyf pasiënte was daar 'n kliniese remissie van die siekte. Vier van hierdie remissies het etlike maande tot 'n jaar of meer geduur.

Verdere verslae oor hierdie nuwe anti-kankermiddel word met groot belangstelling afgewag.

ABSTRACTS

TRANSAMINASE IN DIPHTHERIA

In diphtheria the glutamic-oxaloacetic transaminase is elevated, particularly in severe cases and where there is cardiac involvement. As clinical improvement proceeds, the levels rapidly return to normal even when ECG changes are still to be found.

[Curatolo, D. and Rossi, G. (1959): Gazz. Internaz. Med., **64**, 1727].

THE VITAL CAPACITY IN SMOKERS

Vital capacity is significantly less in smokers than in non-smokers of similar build. On the other hand, residual air is greater among the smokers, although the difference is not always statistically significant.

[Blackburn, H., Brozek, J. and Taylor, H. L. (1959): Ann. Int. Med., **51**, 68].

FAT EMBOLISM

A REVIEW OF ITS CURRENT STATUS

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Fat embolism is defined as the condition which results when liquid oil (or fat) enters the circulating blood and is transported in globules large enough to obstruct the lumen of blood vessels.[1] The condition has been known for many years. Lower is credited with the first experimental observations in 1669, when he produced fat embolism in dogs by the intravenous injection of milk.[2] Lower's classical experiment has been repeated many times by many different observers in animals (Reviews by Vance,[1] Wilson,[2] Scuderi,[3] Holden *et al.*[4]), and inadvertently in humans. For example, cases are quoted by Koch[5] in which liquid fat was injected into a scar with fatal results; by Fibiger[6] in which an individual received 50 c.c. olive oil intravenously with a similar unfortunate outcome; and by Porter[7] in which the injection of 'a very small amount' of olive oil resulted in vasomotor paralysis and severe shock, presumably from embolism of the vasomotor centre. The experimental evidence leaves no doubt that serious symptoms and death may be produced by the intravenous injections of sufficient amounts of neutral fat or mineral oil.[3, 8, 9]

What has to be accurately defined and established are the conditions under which fat embolism occurs as a *purely incidental, symptomless and unimportant finding*, and when a patient's clinical condition or subsequent death may with certainty be ascribed to the condition. The latter type is of particular significance and importance in medico-legal cases.

NATURE OF THE FAT

The first point to consider is the state and amount of fat necessary to produce *significant* degrees of fat embolization. Since arteriolar and capillary blockage is the important pathological feature, the fat must be in globules of sufficient size to impact in these vessels (arterioles 15–40 μ; capillaries 8–15 μ). In most cases, then, the impacted fat globules are in the region of 18–40 μ.[10, 11] They occur as compressed sausage-like bodies conforming to the shape of the vessels, or as undistorted rounded or oval globules. Their demonstration necessitates formalin fixation, frozen sections and subsequent staining with one of the fat soluble bis-azo dyes. The recommended technique is the Oil Red O-Isopropanol method[12] and since the fat emboli are very easily displaced from the vessels, the tissues must be handled with great care and gentleness.

The diagnosis of fat embolism as a significant entity does not rest with the visual observation of impacted fat in the lumina of vessels. Two other questions have to be decided:

(*a*) Are the vessels truly obstructed?

(*b*) Is the vascular obstruction on a wide enough scale to be symptom-producing?

Obstruction of capillaries causes dilatation of the vessels proximal to the emboli. This is a feature which can and should be measured. If it occurs on a wide enough scale it will cause congestion, oedema, petechial haemorrhages and anoxic changes, and these features are usually present when effective obstruction of a capillary bed has been achieved. Unfortunately, oedema and congestion are difficult to assess, and all these changes are non-specific, and may be due to other causes. While the medico-legal pathologist may have difficulty in interpreting their pathogenesis, observation of their presence is necessary to sustain (but not prove) a diagnosis of true obstructive fat embolism. Where a clinical history is available, this should support, with unequivocal signs and symptoms, the fact that effective capillary obstruction by fat emboli has been produced.

Serious obstruction to the blood flow in the pulmonary arteries occurs only when emboli occlude 50% or more of the system.[35] When this has been achieved, there is increased peripheral resistance and anoxia. These factors cause pulmonary hypertension which becomes progressive as a result of arteriolar constriction.[36] This, in turn, results in dilatation of the pulmonary arteries[37-41] and dilatation of the right ventricle (acute cor pulmonale).

Accurate objective proof of an *acute* cor pulmonale at autopsy would be valuable evidence of effective capillary blockage in cases of pulmonary embolism.

A dilated heart is enlarged and the muscle is soft. Acute right ventricular dilatation affects particularly the conus area (so-called toxigenic dilatation)[41] and this becomes prominent, while the chamber itself becomes elongated. Later there is enlargement in a transverse diameter. On opening the chamber the papillary muscles and columnae carneae are flattened and the presence of abundant agony clot can be noted. Sometimes ante-mortem thrombosis is present. In the severer cases, functional incompetence of the tricuspid valve with right ventricular dilatation and agony clot is present, or thrombosis is evident in the dilated auricular appendages. All this is prominent enough in the moderate to severe cases. It can be placed on a more accurate basis by measuring the tricuspid valve and the size of the pulmonary trunk and comparing these with expected normal values. (Tables by Kopsch (1914) and Burwitt (1947) in Gould's *Pathology of the Heart*).[33]

In addition, on histological examination the intercalated discs of the muscle of a dilated heart are much more prominent than usual[42] and minute foci of necrosis may be present in the papillary muscles and subendocardially.[42]

Accurate detailed observations of this type will give positive evidence of an acute cor pulmonale in most cases. Actual measurements of right ventricular and right atrial volume, which should be increased in acute cor pulmonale, are still in the experimental stage and beyond the resources of the average pathologist.

It is essential also to assess the degree of fat embolism. Since in many organs, capillary obstruction has to be widespread before ischaemic effects are produced, the volume of fat reaching the circulation is of importance. The maximum tolerable and minimal lethal doses in the experimental animal are relatively high and average between 0.5–2 g. per Kg. body weight.[3, 8, 9]

It varies also with the nature of the fat. Chaulmoogra oil can apparently be injected intravenously in limited amounts into lepers without effect[1] and liquid fats of suitable particle size can be used with caution for intravenous alimentation.[13] Yet 0.33 g. oleic acid (the main component of bone marrow fat) per Kg. body weight is sufficient to cause death in dogs, while 2.2 c.c. of olive oil per Kg. is necessary to produce the same effect, and the minimum lethal dose of human fat for rabbits is 0.9 c.c.[8, 10] These variations in the type of fat may be due to variation in the local effects. Small amounts of hydrolysed fat produce intense haemorrhagic exudation and the minimum lethal dose is only a fraction of that of neutral fat.[9] Similar observations have been noted with fatty acids and soaps.[14, 15] Oleic acid has been shown to strongly depress the oxygen uptake of certain tumour cells through lysis of the cell membrane.[16] These local effects should be borne in mind in cases where fats foreign to the human body have been injected inadvertently.

Lehmann and Moore[8] calculated after their cotton-seed oil experiments in dogs that a minimum of 120 c.c. would be necessary to cause death in man. They estimated the total fat of the bone marrow as 65 c.c. and concluded that the bone marrow could not be a source of clinical or fatal fat embolism. Since then, Peltier[17] has shown that the tibia and femur each contain 100–200 g. of fat, and Lehmann and Moore's argument[8] becomes untenable.

Since, however, it is seldom possible to assess the amount of fat reaching the circulation, the pathologist in fatal cases should be prepared to assess the number of capillaries and arterioles obstructed in several sections of different parts of an organ. In severe fat embolism two thirds to three fourths of vessels examined should be involved, and arteriolar obstruction should certainly be present. As will be shown, it is vital also to examine not only the lungs but several organs on the systemic side of the circulation, especially the *brain*. In the case of a district surgeon submitting specimens to a laboratory for diagnosis, the best plan, where practicable, is to submit the entire organs. Where this is not possible, the organs, especially the white matter of the brain, should be very carefully scrutinized for petechiae and several representative samples should be forwarded in 10% formol-saline, together with full clinical and autopsy particulars.

It has been suggested[2, 11, 18] that fat globules are fluid and may perhaps permit the passage of blood under pressure even though the vessel appears to be obstructed. This is based on the observation that when a frozen section of a lung is stained with a red dye and observed with a red light source, some erythrocytes are often seen between them and the capillary wall.[2] This, of course, does not prove that blood was flowing through the vessel. The erythrocytes may well be impacted between the embolus and the capillary wall. Nevertheless, the suggestion is enough to indicate that a histological diagnosis of fat embolism must be supported by morphological and clinical evidence to prove that the condition was symptom-producing.

SOURCE OF THE FAT

If fat embolism with capillary bed obstruction sufficient to cause symptoms or death has been observed, the possible sources of the fat must be considered. There are two such sources:

1. Endogenous.
2. Exogenous.

ENDOGENOUS

These include the circulating body lipids and the body stores of adipose tissue.

Blood lipids circulate in close association with plasma proteins in the form of lipoproteins which form particles or macromolecules; 75% of the lipid in the blood plasma is in the form of *beta*-lipoprotein which occurs in the form of spherical particles 180 A in diameter. *Alpha*-lipoproteins are cigar shaped, 300 A long by 50 A wide.[19] Such particles could, of course, never cause vascular obstruction unless considerable flocculation occurs. Normal fasting plasma is clear and contains approximately 100 mg. per 100 c.c. glyceryl esters and 150 mg. per 100 c.c. phospholipid (70–80% is lecithin). A hyperlipaemic plasma will show an increase of glycerides, phospholipid and cholesterol, will become cloudy or turbid and will show the presence of particulate fat, the largest particles measuring 0.5 μ. The total lipid in such plasma rises to 600 mg. per 100 c.c. or more. The particles consist of glyceryl esters and long-chain fatty acids, and migrate with the globulin fraction of the blood.[9] They depend on lecithin for their stability and clump together if treated with lecithinase or other lecithin-hydrolysing factors. Such clumps of lipid are a possible theoretical source for fat embolism. After a fatty meal, particulate glyceride passes via the thoracic duct to the superior vena cava, and 30 mg. of fat in a meal will cause a hyperlipaemia in one hour, increasing to reach a maximum in 3 hours and declining with a fasting state in 5 hours. Particulate glyceride is taken up by the fat depots, but the mechanism of deposition and subsequent mobilization remains obscure. It is also removed in the blood stream by the combined action of heparin and the lipo-clastic enzyme, the clearing factor. Can such a hyperlipaemic state cause fat embolism? There are isolated reports that suggest this is occasionally possible. Wuttig[20] claims to have administered excess cod liver oil orally and to have produced hyperlipaemia and fat embolism. Lehmann and Moore[8] claim that they achieved the same object by feeding excess cream to dogs and when they were hyperlipaemic administered ether (by inhalation and/or intravenously). Fat embolism has been reported as occurring spontaneously in such hyperlipaemic states as diabetes mellitus,[1] pregnancy, renal disease and during the puerperium.[21] Since particulate glyceride can be caused to clump by lecithinase, this has been held to be the cause of fat embolism in *Cl. welchi* infections (lecithinase A).[22, 23] It should be remembered that lecithinases are produced by some animal tissues (pancreas, heart, liver, spleen, brain). Natural enzymes such as glycero-phosphatases and choline phosphatases are also able to hydrolyse lecithin. It is thus theoretically possible for the blood lipids, in hyperlipaemic states particularly, to act as a source of sufficient amounts of sufficiently large fat globules to produce embolism. Whether this occurs to any extent in human cases is not known with certainty. Most authorities scout the possibility.[11, 13] Yet, as will be shown, fat embolism frequently occurs in routine post-mortem examinations in persons dying from natural causes, and the source of the fat in some of these cases remains an enigma. However, Whiteley[24] attempted experimentally to produce clumping of chylomicrons with extracts of organs from post-ischaemic animals without success. Whiteley[24] further suggests that the source of the fat in some minor degree of fat embolism is the liver, and supported his view by producing carbon tetrachloride poisoning in rats.

Body Stores of Adipose Tissue. Trauma to adipose tissue is probably the commonest single cause of fat embolism. The injury must be sufficient to rupture the cell membrane of adipose tissue cells and set free liquid fat; it must also tear veins to permit entrance of the fat and some degree of increased local pressure to force the fat into the vessels is also necessary. Tissue tension around recent fractures and injured areas is increased.[25] Some factor tending to hold the veins open as well would appear to assist the process.[26] All these factors are supplied in fractures of bone. But the condition has also been reported in severe jarring without fracture (fall from a height, a fall on an amputation stump,[1] as a post-operative phenomenon, after severe burns, after labour and after surgical manipulations) and after various degrees of injury to subcutaneous, muscle or visceral fatty regions. The liver may, in severe fatty infiltration, contain large quantities of fat which can apparently be released into the circulation and cause embolism. Thus the condition has been reported in acute and chronic alcoholism, phos-

phorus poisoning, carbon tetrachloride poisoning. Inflammation of fatty tissues on a wide enough scale may be sufficient, e.g. acute osteomyelitis.

EXOGENOUS SOURCES

This is involved in the injection of oily substances into a vein. One of commonest ways in which this is achieved is in criminal abortion. The uterus in early pregnancy is an ideal site for this to happen. Blood supply is abundant and the venous return is by many thin-walled veins. Because of the opening up of direct arteriolar-venous communications, the blood in the uterine veins is returning under pressure, the blood pressure A/V gradient being the same as in an arterio-venous aneurysm. Also the intermittent uterine contractions which occur regularly in pregnancy help to maintain the pressure and to expel the blood and any foreign added substance into the veins. Manipulation of the uterus during the abortion, and the fact that the abortionist often uses a pressure syringe, are other factors whereby almost the whole of the fatty material injected into the uterine wall during pregnancy is rapidly and efficiently transferred to the vascular system. It should be remembered in this connexion that large vacuolated cells containing abundant fat globules are a normal constituent of the chorionic villi. Trauma to these may cause the minor degrees of fat embolism sometimes seen in spontaneous abortion cases. In the toxaemias of pregnancy and in true eclampsia fat embolism may occur from placental degeneration and possibly the liver damage. This, however, is not a factor in early abortions (8th–12th week), as only an occasional case of pregnancy toxaemia has been reported as early as the 10th week.

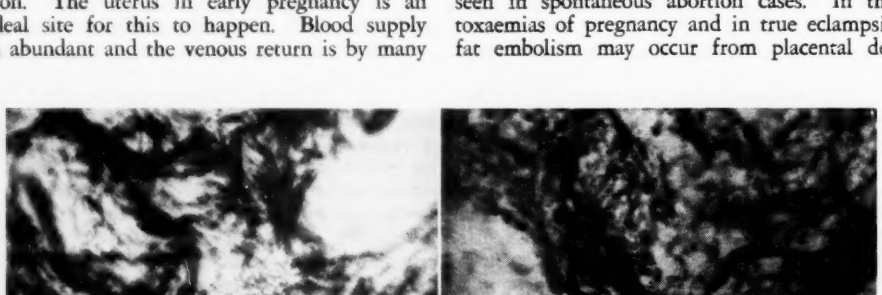

Fig. 1. Section of lung (frozen. 30 μ: Oil-Red O-Isopropanol method).
The section shows a severe degree of fat embolism with marked capillary dilatation. Occlusion on this scale could be duplicated in most fields in sections from base and apex of the lung. Unsuspected during life.

Fig. 2. Section of lung (frozen. 30 μ: Oil-Red O-Propanol technique).
Severe fat embolism of doubtful etiology and source. Unsuspected during life and at routine autopsy.

OCCURRENCE OF FAT EMBOLISM

Most pathologists agree that some degree of fat embolism may be found in routine post-mortem examinations on persons dying from

natural causes, but is rarely severe. Lehmann and McNattin[27] found the condition in 50% of 100 consecutive autopsies; Wright[28] reports the condition in 52 cases of 100 consecutive autopsies; Carrara[29] in 22% of cases dying from cardiovascular disease; Catsaras[30] in 18 of 67 cases of post-influenzal pneumonia. In fact, Vance[1] complains that 'almost all diseases, poisonings and injections to which the body has been subjected have been reported in the literature as having caused fat embolism.'

In a local series of 25 consecutive autopsies, I found pulmonary fat embolism in 10. In 2 cases, the condition was very severe, but had not been suspected during life or at autopsy. The first case was that of an 84-year-old European male who had a gastrectomy for severe haematemesis caused by a florid fatty alcoholic cirrhosis (Fig. 1); the other was that of a case of essential hypertensive arteriosclerosis with congestive cardiac failure and repeated pulmonary emboli (Fig. 2). The milder cases included a variety of disease processes (Table 1).

TABLE 1: MINOR DEGREES OF PULMONARY FAT EMBOLISM IN ROUTINE AUTOPSIES (JOHANNESBURG GENERAL HOSPITAL, 1960).

Cause of Death	*Number*	*Age*	*Source of Fat*
Operative Removal of the Spleen (Angio-Sarcoma)	1	79	Operative trauma
Prostatectomy	1	69	Operative trauma
Essential Hypertension			
(*a*) Cerebral haemorrhage	1	51	?
(*b*) Congestive failure	1	64	?
Rheumatic Heart Disease and Bacterial Endocarditis	1	38	?
Diphtheria and Post-Diphtheritic Paralysis	1	1 year	?
Gas Gangrene	1	70	Tissue breakdown ? Lecithinase
Myeloid Leukaemia	1	45	?

There is no doubt, however, that in injury cases, the incidence is much higher. Vance[1] reported it in 102 cases out of 164 cases examined; he judged it to be severe in 11 and fatal in 3. Robb-Smith[31] regarded fat embolism as a major factor in the cause of death in 25% of 115 accident cases. Sevitt[11] analysed a series of 100 necropsies at the Birmingham Accident Hospital, none of which was suspected of having clinical embolism. Of these 89% had pulmonary fat embolism and 25% systemic embolism.

EFFECTS AND SIGNIFICANCE OF FAT EMBOLISM

Fat globules entering a peripheral systemic vein are transported to the lungs. Depending on their size, they may or may not impact in the lung arterioles or capillaries. Lung capillaries are amongst the largest in the body and particles may transverse them to be transported further by the systemic circulation. Thus there are two important types of fat embolism—*pulmonary* and *systemic* (brain, renal, cardiac).

PULMONARY FAT EMBOLISM

The effects of pulmonary fat embolism are produced as shown in Table 2. Whitson,[32] in a critical review of the subject in 1951, came to the conclusion that the clinical diagnosis of fat embolism should be discontinued, and subsequently Armin and Grant[33] and Sevitt[11, 18] have challenged the concept of pulmonary fat embolism as a symptom-producing lesion in man.

Records at the Birmingham Accident Hospital show that only 25% of patients dying with slight or moderate embolism and 15% of those dying with severe embolism had respiratory symptoms. Respiratory complications such as cough, dyspnoea, bronchitis, pneumonia, atelectasis and infarction were as frequent in injured patients with slight to moderate fat embolism as they were in severe cases. Sevitt[11, 18] concludes that pulmonary embolism is rarely responsible for cardio-respiratory embarrassment and this must be related to the large functional reserves and enormous capillary bed within the lungs. Sevitt[11] considers that the amount of fat reaching the lungs even in severe post-traumatic embolism is only a fraction of what would be required to produce effective capillary and arteriolar blockage, and that pulmonary embolism is never responsible for death, even in patients with shock or haemorrhage. Sevitt's[11, 18] proposition will require further study. It is based on a considerable experience of post-traumatic cases where the amount of fat gaining access to the systemic circulation may not only be limited but may be slowly released after hours or days. It does not neces-

phorus poisoning, carbon tetrachloride poisoning. Inflammation of fatty tissues on a wide enough scale may be sufficient, e.g. acute osteomyelitis.

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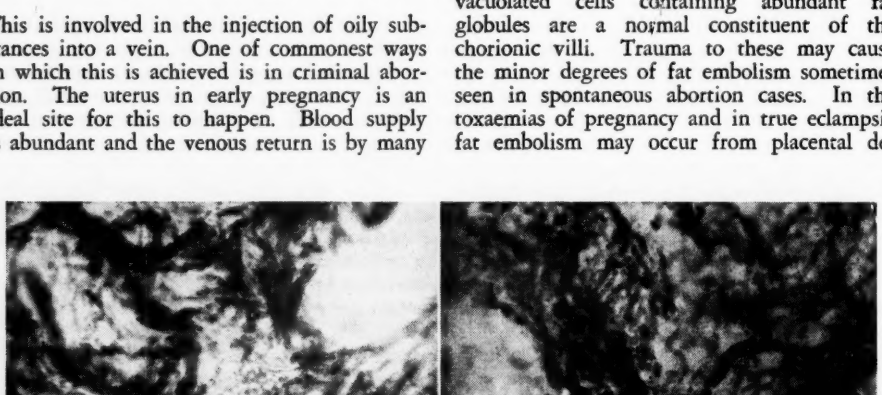

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(*b*) Congestive failure	1	64	?
Rheumatic Heart Disease and Bacterial Endocarditis	1	38	?
Diphtheria and Post-Diphtheritic Paralysis	1	1 year	?
Gas Gangrene	1	70	Tissue breakdown ? Lecithinase
Myeloid Leukaemia	1	45	?

There is no doubt, however, that in injury cases, the incidence is much higher. Vance[1] reported it in 102 cases out of 164 cases examined; he judged it to be severe in 11 and fatal in 3. Robb-Smith[31] regarded fat embolism as a major factor in the cause of death in 25% of 115 accident cases. Sevitt[11] analysed a series of 100 necropsies at the Birmingham Accident Hospital, none of which was suspected of having clinical embolism. Of these 89% had pulmonary fat embolism and 25% systemic embolism.

EFFECTS AND SIGNIFICANCE OF FAT EMBOLISM

Fat globules entering a peripheral systemic vein are transported to the lungs. Depending on their size, they may or may not impact in the lung arterioles or capillaries. Lung capillaries are amongst the largest in the body and particles may transverse them to be transported further by the systemic circulation. Thus there are two important types of fat embolism—*pulmonary* and *systemic* (brain, renal, cardiac).

PULMONARY FAT EMBOLISM

The effects of pulmonary fat embolism are produced as shown in Table 2. Whitson,[32] in a critical review of the subject in 1951, came to the conclusion that the clinical diagnosis of fat embolism should be discontinued, and subsequently Armin and Grant[33] and Sevitt[11, 13] have challenged the concept of pulmonary fat embolism as a symptom-producing lesion in man.

Records at the Birmingham Accident Hospital show that only 25% of patients dying with slight or moderate embolism and 15% of those dying with severe embolism had respiratory symptoms. Respiratory complications such as cough, dyspnoea, bronchitis, pneumonia, atelectasis and infarction were as frequent in injured patients with slight to moderate fat embolism as they were in severe cases. Sevitt[11, 13] concludes that pulmonary embolism is rarely responsible for cardio-respiratory embarrassment and this must be related to the large functional reserves and enormous capillary bed within the lungs. Sevitt[11] considers that the amount of fat reaching the lungs even in severe post-traumatic embolism is only a fraction of what would be required to produce effective capillary and arteriolar blockage, and that pulmonary embolism is never responsible for death, even in patients with shock or haemorrhage. Sevitt's[11, 13] proposition will require further study. It is based on a considerable experience of post-traumatic cases where the amount of fat gaining access to the systemic circulation may not only be limited but may be slowly released after hours or days. It does not neces-

sarily apply to cases where oil has been injected intravenously, especially where the oil is one foreign to the human body. The response of the cardio-respiratory organs to such an *acute* episode may well be different. Cases of acute respiratory embarrassment following such an injection are described in the literature. Experimentally, slow intravenous injection of arachis oil (0.05 ml. per 10.0 g.) in the normal rat is followed by a gradual rise in the respiratory rate to about 2–3 times the resting rate. If the fat is injected rapidly, there is often an initial period of apnoea for about 5–10 seconds, after which the respiratory rate is resumed at a raised level. Larger doses of 0.1 ml. per 100 g. are followed by prolonged apnoea and then a few convulsive respiratory movements preceding death.[24]

In any case, in view of these doubts it becomes imperative, where fat embolism is to be regarded as a cause of death, to demonstrate the presence of systemic embolization, especially cerebral.

TABLE 2: PULMONARY FAT EMBOLI

Multiple Fat Emboli in the Lung Effective Capillary and Arteriolar Blockage			Systemic Embolism (Cerebral, Renal, Cardiac)	
Local Effects	Fat Globules in Sputum	Anoxia	Pulmonary Hypertension	Decreased Input Volume to Left Ventricle
Petechiae	Blood in Sputum	Cyanosis	Dilatation of the Pulmonary Artery	Compensatory Tachycardia; Peripheral Vaso-constriction
Oedema	Apical and Marginal Emphysema	Respiratory Distress	Acute Cor Pulmonale	Acute Left Ventricular Output Failure
Congestion		Arterial O_2 Fall		Fall in Blood Pressure
Focal Atelectasis		CO_2 Retention		Pallor
		Systemic Anoxia		Syncope, etc.

SYSTEMIC FAT EMBOLIZATION

After traversing the lungs (small-size emboli; A/V shunts) fat emboli reach the systemic circulation. Normally 25% of left ventricular output goes to the brain and another 25% to the kidneys. These organs, therefore, are predominantly involved in systemic fat embolism, but other sites may, of course, be reached (heart, liver, spleen, skin).

Cerebral fat embolism is of paramount importance. In contrast to the lungs, only small amounts of fat are necessary to produce symptoms or death, and the fact that fat emboli cause capillary obstruction has not been disputed in this organ. Cerebral fat embolism is usually manifested morphologically by petechial haemorrhages, oedema and anoxic changes, although these may be very ill-defined or absent; functionally by stupor or coma, epileptiform attacks, pareses and a variety of other neurological or mental disturbances. Systemic fat embolism of the skin leads to a petechial rash which can be of immense value in diagnosis (skin biopsy will remove any doubts). Fat embolization of the kidney (glomerular capillaries) would have to be very widespread to produce renal insufficiency, but fat globules may occur in the urine. The tests for this, however, are unreliable. Sevitt[11] has advocated needle biopsy of the kidney in special cases, e.g. obscure post-traumatic coma.

Clinically significant cerebral embolism occurs in from 0.8%[10] to 15.0%[34] of miscellaneous injury cases. In autopsy cases it has been demonstrated in 1.8–20% of accident cases terminating fatally, depending upon the degree and site of injuries.

In Sevitt's series[11] all cases of systemic fat embolism had pulmonary emboli, especially when this was severe; but only a fraction of cases with pulmonary fat emboli had systemic embolism. Sevitt[11] subdivides systemic embo-

lism into the fulminating type (death in coma in 1–2 days), the classical type with respiratory and cerebral symptoms and petechial skin rash (this carries a high mortality) and incomplete or partial types in which cerebral and/or respiratory effects are absent (low mortality). The position regarding myocardial embolism is being further studied. Sevitt[11] suggests that the importance of this entity has been exaggerated.

In essence, then, pulmonary fat embolism by itself has lost importance as a clinical or fatal entity; systemic embolism, especially cerebral, is the major issue. However, the subject cannot be regarded as closed with this current conclusion. Other factors may well cause a reassessment of the whole picture. For example, Green and Stoner[35] showed that when adenosine triphosphate was injected with fat, smaller doses of the latter proved fatal and the emboli were seen as large droplets in the arterioles not in capillaries, and Whiteley[24] showed that the presence of muscle ischaemia reduced the intravenous dose of fat needed to cause symptoms or death.

Nevertheless, it would be foolish not to concede that massive fat embolism is necessary to produce respiratory embarrassment, and that fatal fat embolism is probably exclusively due to cerebral involvement.

SUMMARY

1. The current status of fat embolism as a symptom-producing lesion is reviewed.

2. It is stressed that the visual observation of fat embolism must include a critical assessment of its severity and must be supported by morphological and clinical evidence of effective vascular obstruction.

3. It is important to realize that to invoke fat embolism as a cause of death, evidence of cerebral fat embolism will almost certainly be required.

4. The diagnosis of fat embolism with certainty during life requires in difficult or atypical cases skin or renal biopsy.

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MEDICO-LEGAL SECTION

AGREEMENT BY WORKMEN TO PAY FEES IN EXCESS OF AMOUNT PRESCRIBED IN TERMS OF THE WORKMEN'S COMPENSATION ACT

McDONALD v. ENSLIN*

As the prohibition in section 79 of the Workmen's Compensation Act, 30 of 1941, against claiming an amount in respect of medical aid in excess of that prescribed in the section was enacted solely for the benefit and protection of the workman, and as there is nothing in the Act to preclude it, the workman is entitled to waive the provisions of section 79. He is therefore entitled to enter into a valid contract whereby he undertakes to pay an amount in excess of what is prescribed for medical aid in terms of the section, i.e. to pay the difference between the amount payable to a medical practitioner by the Commissioner and the medical practitioner's actual fee.

Appeal from a decision in a magistrate's court. The facts appear from the reasons for judgment.

H. J. O. van Heerden, for the appellant: Indien art. 77, 79 en 80 van Wet 30 van 1941 (soos gewysig) saamgelees word, volg dit dat 'n werksman nie aanspreeklik is vir mediese koste nie. Ingevolge die oorspronklike artikels sou hy slegs aanspreeklik gewees het indien die koste £100 oorskry het, maar dan alleen indien bedoelde koste aan die vereistes van art. 79 beantwoord het. Dit is derhalwe duidelik dat respondent in die onderhawige saak geen bedrag van appellant kon verhaal het nie; *a fortiori* dus ook nie die verskil tussen sy fooie en die bedrag deur die Kommissaris aan hom uitbetaal nie. Aangesien die genoemde Wet daarop gerig is om te verseker dat fooie ten opsigte van mediese behandeling nie van 'n werksman verhaal word nie, is enige ooreenkoms wat meebring dat bedoelde fooie wel aldus verhaal kan word, nietig; vgl. *Davidson* v. *Honey,* 1951 (4) S.A. 257. Daar is immers geen basiese verskil tussen die geval waar die Wetgewer bepaal het dat geen hoër huurgelde as die deur die Huurraad bepaal, van 'n huurder verhaal mag word nie, en die geval waar voorgeskryf word dat 'n werksman nie aanspreeklik is vir fooie nie. Dit was die bedoeling van die Wetgewer dat werkslui, op wie se bedrywighede die ekonomiese struktuur primêr berus, ten volle gevrywaar moet wees van skade wat hulle as gevolg van ongevalle ly. Enige ooreenkoms wat in stryd met die bedoeling is, moet derhalwe in stryd met die openbare beleid wees; vgl. *Froneman* v. *Lartz,* 1949 (1) S.A. 977; *Universal Negro Improvement Association* v. *Levine,* 1949 (2) S.A. 351.

H. C. J. Flemming, for the respondent: In Wet 30 van 1941 (soos gewysig) word vergoeding vir geneeskundige behandeling as 'n afsonderlike begrip gebruik teenoor skadeloosstelling. 'n Werksman is geregtig om persoonlik onkostes vir mediese hulp aan te gaan. Afgesien selfs van die doel van die Wet waarna hieronder verwys word, is dit op die bewoording van Hoofstuk VIII en veral art. 79 duidelik dat 'n werksman vir mediese koste aanspreeklik gehou kan word, omdat dit logies volg uit die feit dat die Kommissaris nie vir alle mediese koste aanspreeklik is nie maar slegs vir 'n deel daarvan. Daar bestaan gevolglik geen rede waarom nie aan die uitdruklike woorde van die Wet gevolg gegee sal word nie, nl. dat wanneer van 'n werksman geëis word sal " geen groter bedrag dan die koste . . . tarief vasgestel . . . op . . . 'n werksman . . . verhaal word nie ". Vir appellant se verweer om te slaag moet hy dus beweer dat die verskil tussen die bedrag deur die Kommissaris betaal en die bedrag deur respondent geëis die tarief oorskry of andersins moet hy beweer en bewys dat ten opsigte van die besondere behandeling, daar geen tarief bestaan nie en dat dit die verskil 'n oorskryding daarstel van die bedrag deur die Kommissaris billik geag. Die doel van die onderhawige Wet is om die aanspreeklikheid van werkgewers, en nou ook die Kommissaris in te stel en te reguleer en dienooreenkomstig die werksman se aanspraak op vergoeding te wysig. Die Wet stel 'n aanspreeklikheid vir skade daar wat nie op skuld berus nie. Verder kan as oogmerk van die Wet genoem word beskerming van die werksman se arbeidsvermoë wat insluit herstel daarvan op die bes moontlike manier so gou as moontlik. Dit is om hierdie doel wat Hoofstuk VIII dien. Hoofstuk VIII is nie in alle opsigte op dieselfde voet as die bepalings ten opsigte van skadeloosstelling nie en moet interpreteer word met genoemde oogmerk voor oë. Op die be-

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woording van die Wet self is daar geen aanduiding wat dit bo twyfel stel dat 'n werksman nie van sy beskerming ten opsigte van mediese onkoste kan afstand doen nie. Daar word geen beperking gelê op afstanddoening in die spesifieke geval uit hoofde van " public policy " nie omdat hierdie nie 'n beskerming is wat gegee is in die openbare belang nie. Waar beskerming ten gunste alleen van 'n klas persone is en nie vir die publiek in die algemeen nie, is 'n Wet in die algemeen nie in die openbare belang nie; sien *Froneman* v. *Lartz, supra* te bl. 985; *Barrett and Glynn* v. *Davidson,* 1916 T.P.D. 42. Ook hierdie tipe beskerming is in die belang van die indiwidu; sien *Morrison* v. *Anglo Deep Gold Mines Ltd.,* 1905 T.S. 775. Indien daar enige twyfel bestaan, sal ons Howe die uitleg volg wat die minste met die gemene reg inmeng; sien Steyn, *Uitleg van Wette,* bl. 90; veral in die lig van die reël dat " Rights are not to be held to have been taken away save by express or necessary implication " soos weer gestel in *Wellworths Bazaars, Ltd.* v. *Chandlers,* 1947 (2) S.A. te bl. 43. Al sou afstanddoening van die beskerming by die aangaan van die kontrak strydig wees met die eintlike doel van die Wet is afstanddoening tydens die bestaan van die kontrak nie op dieselfde voet nie en heeltemal geldig; sien *Froneman* se saak, *supra; de Vos* v. *Monnik & Visser,* 1944 C.P.D. te bl. 36; *Village Deep Gold Mining Ltd.* v. *O'Brien,* 1912 T.P.D. te bl. 743.

van Heerden, in repliek.

Cur. adv. vult.

Postea (February 25th).

POTGIETER, J.: In the court *a quo* respondent (hereinafter called plaintiff) sued appellant (hereinafter called defendant) for an amount of £10 10s. being the balance owing in respect of professional services rendered. It appears from the further particulars to the summons that on the 6th June, 1957, plaintiff undertook to render certain medical treatment to defendant at a fee of 50 guineas. When plaintiff's services were first requested defendant intimated to plaintiff that he was to be treated as a private patient. It later transpired that defendant was a patient under the Workmen's Compensation Commissioner. During September, 1958, the latter paid an amount of £42 to plaintiff leaving a balance of £10 10s.

Defendant filed a special plea and alternatively a plea on the merits. The special plea runs as follows:

" Defendant denies that he is indebted to the plaintiff as alleged and says that plaintiff is not entitled to recover the amount charged in excess from the defendant. The defendant says that in terms of sec. 79 of Act 30 of 1941 the plaintiff has no right to claim the amount paid by the Workmen's Compensation Commissioner.

Wherefore defendant prays that plaintiff's claim be dismissed with costs."

Plaintiff then filed a replication the relevant paragraph whereof reads as follows:

" Plaintiff denies that he is not in this case entitled to charge an amount in excess of that assessed by the Workmen's Compensation Commissioner as the parties hereto agreed in a valid and binding agreement that the defendant would pay to plaintiff the difference, if any, between the amount paid by the Workmen's Compensation Commissioner and our client's fees for professional services rendered."

No evidence was led in the court below but apparently the matter was argued by both parties on the assumption that the facts alleged in the summons, the further particulars, the special plea and the paragraph in the replication quoted above were accepted as proved. Counsel who appeared before us in the appeal also argued the appeal on that basis.

The magistrate entered judgment in plaintiff's favour with costs and defendant now appeals against that judgment.

It seems to me that the appeal involves the crisp question whether a workman is entitled to enter into a valid and binding contract whereby he undertakes to pay an amount in excess of what is prescribed for medical aid in terms of sec. 79 of the Workmen's Compensation Act, 30 of 1941.

This again involves the question whether a workman is entitled to waive the provisions of sec. 79 which preclude the recovery of an amount in excess of that prescribed by the Commissioner or in the absence of a charge having been fixed in excess of the charge deemed by the Commissioner to be reasonable.

Apart from cases where the statute expressly or by necessary implication prohibits waiver the general rule is that any person can enter into a binding contract to waive the benefits conferred upon him by law for his sole benefit and the rule is expressed by the maxim of law, *quilibet potest renuntiare iuri pro se introducto.* But where public as well as individual interests are concerned, in other words where public policy demands the observance of a statute, then the benefit of its provisions cannot be waived by the individual, because he is not the only person interested. (See *Morrison* v. *Anglo Deep Gold Mines Ltd.,* 1905 T.S. 775 at p. 781; *Froneman* v. *Lartz,* 1949 (1) S.A. 977 (O) at p. 981.)

Now sec. 79 of the Act (as amended by sec. 22 of Act 51 of 1956) reads as follows:

"(1) The commissioner or the employer individually liable, as the case may be, shall for a period not exceeding two years from the date of the accident defray the reasonable expenses incurred by or on behalf of a workman in respect of medical aid necessitated by an accident.

(2) Where, in the opinion of the commissioner, further or special medical aid in addition to that referred to in sub-sec. (1), will reduce the disablement from which the workman suffers, he may defray or direct the employer individually liable to defray, as the case may be, the expenses incurred in respect of such medical aid."

Sec. 79 reads:

"Fees for medical aid to be prescribed. Payment for medical aid shall be in accordance with the scale prescribed from time to time by the commissioner after consultation with the Medical Association of South Africa (British Medical Association), and no claim in excess of the charges fixed by that scale or, if no charge has been so fixed, in excess of the charges deemed by the commissioner to be reasonable, shall lie against the commissioner, or any workman or his employer in respect of any such medical aid."

Sec. 32 expressly provides that any contract whereby a workman relinquishes any right to compensation under the Act shall be null and void. In terms of the provisions of the Act medical aid is not included in the word *compensation* and is dealt with separately. There is no other provision in the Act similar to sec. 32 dealing with medical aid. Nor can I find anything in the Act which indicates that waiver of the provisions of sec. 79 is by necessary implication prohibited.

The only problem then to decide is whether the prohibition against claiming an amount in excess of that prescribed in sec. 79 is a provision conceived solely for the benefit of the workman or whether there is any public interest involved.

The provisions dealing with compensation for injuries to a workman are to my mind clearly enacted solely for the benefit of the workman (cf. *Griffiths* v. *The Earl of Dudley*, (1882) 9 Q.B. 357 at pp. 362, 363). If it were otherwise it would have been unnecessary to enact sec. 32 dealing with the prohibition of a waiver in respect of compensation for injuries.

In respect of medical aid which becomes necessary as a result of injuries to a workman, the position is that the Commissioner or the employer, as the case may be, must pay the reasonable expenses incurred by the workman subject to the limitation that they are so liable for a period not exceeding two years from the date of the accident. This provision seems to me clearly also to be conceived solely for the benefit of the workman. In terms of sec. 79, read with sec. 77, the Commissioner or the employer individually liable, as the case may be, is only liable to pay in accordance with the scale prescribed by the Commissioner or if no charge is fixed, then an amount which the Commissioner deems reasonable. The section then goes on to provide that not only shall no claim lie against the Commissioner or employer for any excess of those amounts but affords a further protection to the workman by also prohibiting any claim against him individually for such excess. *A fortiori* this provision seems to be clearly for the benefit only of the workman.

Mr. *van Heerden*, for the appellant, urged that the provisions dealing with medical aid are primarily enacted for the public benefit inasmuch as it is in the public interest that when a workman has been injured he must receive medical attention immediately so as to be able to go back to work as soon as possible. I do not think, however, that the provisions regarding medical aid were introduced for that reason. It seems to me that they were enacted solely for the benefit and protection of the workman. To a certain extent it may be a matter of public expedience to protect and to benefit workmen but if such an Act is passed it is surely not passed for the benefit of the State.

In the case of *Barrett and Glynn* v. *Davidson*, 1916 T.P.D. 42 at p. 43, it was held by WESSELS, J. (as he then was), that the Moratorium Act was passed for the benefit of the individual and that its provisions could be waived. If the Moratorium Act was not passed for the benefit of the State *a fortiori* to my mind these provisions of the Workmen's Compensation Act were not enacted for the benefit of the State.

I come to the conclusion, therefore, that defendant was entitled to enter into a valid and enforceable agreement to pay the difference between the amount payable by the Commissioner and plaintiff's actual fee in spite of the provisions of sec. 79.

The appeal is accordingly dismissed with costs.

KLOPPER, J., concurred.

Appellant's Attorneys: *Symington & de Kok.*
Respondent's Attorneys: *Heath & Venter.*

A CLINICAL TRIAL OF SELVIGON

A NEW ANTITUSSIVE

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and

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Although there are many antitussive preparations which the practitioner can prescribe for his patients, opium (or one of its derivatives), is still the only really reliable and effective drug. Codeine phosphate, either alone or in combination with less active drugs, is most widely used and, when given in adequate doses, is certainly efficacious. There are, however, certain associated disadvantages. Constipation, especially in the elderly, may be a difficult problem and, in the 'chronic cougher,' addiction is, of course, not unknown. The difficulty of assessing the effects of an antitussive is due to the sometimes 'embarrassing' fact that many patients will stop coughing whether they have been treated or not. There is also a big psychological element to be considered and in some patients with chronic disease of the bronchial tree and lungs no antitussive can be efficacious until the cough centre is depressed to dangerous levels. Sometimes a cough may be suppressed with a subsequent accumulation of bronchial secretions, with obvious ensuing disadvantages. Cough mixtures are seldom prescribed with any degree of confidence by the doctor, although when he has to suppress a cough he can still do so with heroin, which, however, has now come to be regarded with grave distrust because of its addictive properties. What is needed is a drug which will not be habit-forming and will not produce side effects which would limit its continued use.

Recently, a new antitussive, Selvigon, was made available for trial. It was claimed that it suppressed coughing without interfering with the expectoration of bronchial secretions. It was also claimed that Selvigon had not given rise to any side effects and was consequently very safe. Gulden,[1] Libal[2] and Platt *et al.*[3] have published results on the use of Selvigon. They all asserted that this preparation was a potent antitussive and as good as, if not better, than codeine without the disadvantages associated with the latter drug, especially in elderly patients. In the winter of 1960 Selvigon was given a clinical trial in 3 separate practices and the combined results form the substance of this paper.

METHODS AND MATERIAL

No special selection of patients was made for this trial. Any patient who was coughing so that his comfort was disturbed was given Selvigon. Some of the patients were suffering from an acute upper respiratory tract infection, whereas others were chronic coughers with an exacerbation due to a superimposed infection.

The evaluation of the effects of treatment was difficult in some patients, for antibiotics and other drugs were prescribed if they were indicated. However, in the assessment of the results, these and several other factors were considered. Many patients often cease coughing within a day or two even if treatment is not given; whereas patients with chronic bronchitis, for example, are not likely to be cured of their cough after being treated for only one week. Special record cards were available on which, at the end of each day, the severity of the cough was noted by symbols previously agreed upon. The key employed was, 'no cough' = 0, 'moderate cough' = + and 'severe cough' = ++. By questioning the patient and his relations, and by the investigator's own observations, it was possible to obtain an evaluation of the patient's cough after 7 days' treatment.

The assessment for the purpose of this investigation was then made as follows:

(A): 'Very good'; the cough ceased before the end of 3 days' treatment in acute cases;

(B): Patients with chronic cough were markedly ameliorated and there was a conspicuous difference because of taking the drug; and

(C): In patients with excessive bronchial secretion the cough was improved but the expectoration of sputum, however, was not suppressed.

By 'good' was meant that the factors mentioned above were not conspicuously improved but the results were still most satisfactory. A 'fair response' was interpreted as improvement noted but the patients were still coughing, although less than before. Where the results were recorded as 'no effect,' it meant that the antitussive did not have any effect on the cough, or else was considered not to have had any significant part in relieving the patient of the cough. This same assessment of the cough was used by other investigators in the trial for the purposes of comparison.

DOSAGE

Two preparations of Selvigon were available:

(1) A liquid form—adult dose, 15–25 drops *t.i.d.*; each ml. of the preparation contained 40 mg.

(2) Tablets also could be prescribed, 1–2 *t.i.d.*; each tablet contained 20 mg. of Selvigon.

The dose was varied for children. Treatment was given for a maximum of 7 days to each patient but, if the cough stopped, treatment was stopped too. The assessment of the results was thus made over a period not exceeding 7 days' treatment.

RESULTS

Table 1 shows the results of treatment in 90 patients. There were at least another 25 patients treated, but only in 90 were we in the position to evaluate the results with any confidence. Sixty-four responded most satisfactorily to treatment, of whom 45 were recorded as 'very good' and 19 as 'good.' In 15 patients, the results were 'fair.' In 11, no claim could be made that Selvigon had produced any effect whatever.

In the *acute bronchitis* patients, 27 of 30 were satisfactory. In the *chronic bronchitis* group, 16 reponded satisfactorily and 8 unsatisfactorily. In the *acute tracheitis* group, 16 of 20 were satisfactory. In the remaining 16 patients, the *miscellaneous group,* from the very nature of the diseases treated, very good results could not have been expected. In this group, 3 patients suffering from *whooping cough* showed some improvement, 2 of whom were recorded as 'good.' There were 13 patients suffering from *bronchiectasis, asthma with bronchitis, bronchitis with emphysema, carcinoma of the bronchus* and 1 with *cor pulmonale.* The patient with cor pulmonale and the patient suffering from bronchiectasis failed to respond at all, whereas the other 11 did respond to a certain extent.

There was no difference between those taking the tablets or the liquid preparation. As a rule, the children were given the liquid preparation. There were no side effects.

DISCUSSION

Most of the patients suffering from acute bronchitis and acute tracheitis had been coughing for from 3–15 days before treatment was begun. The chronic bronchitic patients had mostly coughed for more than 12 weeks and some of them had been sufferers for many years. The best results were seen in the acute bronchitis and the acute tracheitis patients. After treatment patients were able to sleep undisturbed by coughing and, almost without exception, this was commented on by all throughout the trial. There was no difficulty in expectoration and it appeared that Selvigon could sup-

TABLE 1: THE EFFECT OF SELVIGON ADMINISTRATION ON COUGHING

Diagnosis	*Number of Patients*	*Results*			
		Very Good	*Good*	*Fair*	*Poor*
Acute Bronchitis	30	24	3	2	1
Chronic Bronchitis	24	9	7	5	3
Acute Tracheitis	20	12	4	2	2
Miscellaneous*	16	0	5	6	5
Total	90	45	19	15	11

Satisfactory: 45+19=64
Unsatisfactory 15+11=26

*Chronic bronchitis with asthma; Chronic bronchitis with emphysema; Chronic bronchiectasis; Carcinoma of the bronchus; Cor pulmonale; Whooping cough.

press the cough reflexes sufficiently to make the patient comfortable without interfering with expectoration when this was required.

There is no doubt of the necessity for an antitussive, as persistent coughing which defies treatment may produce exhaustion, especially in the aged. If it is possible to control this hacking and exhausting cough and thus promote sleep at night without at the same time interfering with expectoration, then the desiderata of a good antitussive are achieved.

In this trial on Selvigon, 90 patients were treated and the first 3 groups (a total of 74 patients) can be considered as the main group for evaluating the drug. Sixty-four of these 90 patients responded satisfactorily. This result was encouraging and clearly indicative of the value of Selvigon.

No side effects were seen in any patient and it appears that the preparation is safe and efficient and, especially in tablet form, a most convenient and satisfactory method of treatment.

SUMMARY

1. Ninety patients suffering from cough requiring therapy were treated with Selvigon.

2. Sixty-four patients responded satisfactorily. Forty-five were recorded as 'very good' results and 19 as 'good.' Of the remaining 26 patients, 15 were recorded as 'fair' and in 11 there was no response at all.

3. Selvigon is a safe and efficacious antitussive and should be of distinct value.

We wish to thank Smith Kline & French Laboratories Ltd. for the supply of Selvigon.

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ADAM'S OPERATION: PARTIAL ADRENALECTOMY?

A SURGICO-THEOLOGICAL SPECULATION

S. LEVIN, M.B. (RAND), M.R.C.P. (EDIN.), D.C.H.
Johannesburg

> 'And the Lord caused a deep sleep to fall upon Adam, and he slept; and he took one of his ribs, and closed up the flesh instead thereof . . . And Adam said, This is now bone of my bones, and flesh of my flesh . . .'
>
> *Genesis* 2:21, 23

It is not to be imagined that the Almighty was content with a minor procedure such as a rib resection. As a preliminary to a partial adrenalectomy, however, much about Genesis becomes more clear, and it is possible to achieve some sort of synthesis between myth and medicine.

Forgetting for the moment about theology, one may consider the Adam and Eve fable purely from the point of view of anatomy and physiology. One need not accept literally the statement that only one rib was removed; indeed Adam declares ('bone of my *bones*') that rather more ribs were utilized.

Man has 2 pairs of incomplete ribs, woman possessing the excised portions: four half-ribs; but Adam claimed that not only were Eve's bones from his, but that she was also flesh of his flesh. Clearly some other tissue was also transplanted, a tissue presumably more vital than mere bone, and a good deal of evidence favours the adrenal gland.

By means of bilateral posterior incisions, subsequently healed without leaving any mark, the Great Surgeon excised portions of 2 pairs of ribs from Adam, together with sections of the underlying adrenals, and therefrom fashioned his mate.

The adrenal was the obvious organ to employ for making woman. It is the only structure common to man and woman that secretes both male and female hormones. Moreover, the gland positively looks as though it has been sliced by a Secret Knife; unlike any other organ in the body, the adrenal is not rounded, not curved, not complete; with its flat surfaces and sharp edges it leaves little doubt that it has been cut and trimmed into geometrical shape, whereas all other organs have been permitted to keep their rotundity.

THE FORBIDDEN FRUIT

There being only one androgynous gland in the male body, God formed woman from the adrenal, and then, exercising good post-operative care, warned them both against partaking of the forbidden fruit, 'for in the day that thou eatest thereof thou shalt surely die' (2:7). There was good reason for such advice, but it involves a more lengthy consideration of the character of the forbidden fruit.

Legend favours the apple for this unhappy role, or even the fig, but minor legends have also espoused the cause of the banana, and if, as appears likely, *Homo sapiens* dawned in Africa, then the banana is at least indigenous. The ingestion of bananas is known to result in the increased excretion in the urine of catecholamines and, indeed, noradrenaline, one of these amines, is actually present in bananas. Having performed the most delicate of operations, and having noted that the physiology of His creations was stable immediately post-operatively, the Great Surgeon wisely cautioned against bananas lest the ingestion of large amounts of noradrenaline upset the homeostatic mechanisms so recently stabilized. Indeed the possibility of amine-induced hypertension, with its possibly lethal complications, had to be entertained. But the forbidden fruit did not upset the biochemical resilience of Adam and Eve, and the dire prognosis was not fulfilled. They lived for many hundreds of years. Such was the Almighty's concern about upsetting adrenal physiology that subsequent Law placed a taboo on the adrenal gland and forbade it as an article of diet (Leviticus 3:4, 15, 16).

SIAMESE TWINS SUNDERED

The ancients of millennia long forgotten were troubled by man's origin. The rabbis, in fact, echoed an earlier Persian myth that Adam was originally a bisexual creature, a Siamese twin, being joined to Eve at the back, and that God sundered them through the connecting tissue —Adam's rib—to make two individuals. As evidence thereof, one can point to a variant of the creation epic: 'Male and female created He them; and blessed them, and called *their* name Adam . . .' (5:2). This plainly contradicts the tale of the rib, suggests rather the presence of a bisexual Siamese being, later divided. Genesis 1:27 attempts a synthesis: 'So God created man in His own image, in the image of God created He him, male and female created He them.' The compromise is not successful, suggesting merely that God also partook of androgynous characteristics.

But the contradictions vanish when it is theorized that the original Adam merely had the propensity for Eve within him, not a real Eve tacked on to his back. Indeed, such is excluded by Genesis 2:18, 'It is not good that man should be alone.' Adam harboured within his body a tissue secreting feminine hormones, and from which a feminine body could properly be constructed, so it is that 'male and female (in adrenal propensity) created He them . . . and called their name Adam . . .' This can then be reconciled with the story of the rib, for the latter deals only with the method of approach to the adrenal glands.

LILITH

Such a theory solves another associated myth: the belief that Adam's first wife was the ghostly Lilith, and that from their coupling were formed all the demons and evil spirits of the Underworld. There being as yet no material female, the coupling with Lilith was an experiment, and the offspring, like their mother, were not quite solid flesh. Eve was only fashioned rather late in the day, when it was realized that it was not good that man should be alone. At this time Adam might have endured Lilith for maybe a century. Certainly the Bible gives us no indication of such time periods, mentioning male and female in the same initial sentence (1:27), but then the narrative of Genesis is not necessarily in chronological order, only in spiritual order (whatever that may mean).

Accordingly, when Eve was formed, Adam dispensed with Lilith, recognizing in Eve a kindred flesh and bone. So, 'Adam lived an hundred and thirty years, and begat a son in his own likeness, after his image . . .' (5:3), from which the inference is drawn that prior to this period he had sired offspring that were not in his own likeness and image, namely demons. However, Genesis 5:3 refers to his third son Seth, so that Cain and Abel must be excluded on other grounds: Cain on the grounds that he resembled Eve, and not his father, and Abel on the grounds that he resembled neither, and was possessed of rather unique qualities, being in fact the first individual to undergo a physical and moral mutation. Such a suggestion might challenge the status of his parents as the first to be faultless and without sin—at any rate before the Fall.

NOTES AND NEWS : BERIGTE

THE FIFTH WORLD ASSEMBLY OF THE ISRAEL MEDICAL ASSOCIATION

This meeting will be held from 14–25 August 1961 under the patronage of the Israeli Minister of Health. Sessions are scheduled to take place in Jerusalem, Haifa and Tel Aviv.

Prof. J. Landau is Chairman of the Assembly, which marks the jubilee of the Israel Medical Association.

* * *

ELI LILLY MEDICAL RESEARCH FELLOWSHIP (SOUTH AFRICA) 1961

1. Applications are invited from suitably qualified medical practitioners for the Eli Lilly Medical Research Fellowship (South Africa).

2. The Fellowship is for the purpose of medical research and is not intended for post-graduate clinical study. It is available for one year.

3. The value of the Fellowship is 3,600 United States dollars for one year and, in addition, travelling expenses will be allowed, based on a travel budget to be submitted by the Fellow. This will cover the cost of travel and incidental expenses from the place of residence of the Fellow to the approved place of study in the United States of America, as well as the return journey.

4. Other things being equal, preference will be given to candidates under 40 years of age.

5. Any medical practitioner *registered* in South Africa will be eligible for this award.

6. There will be no discrimination for the award on grounds of race, colour, creed or sex.

7. The candidate must submit evidence of his capacity to do original research work.

8. The candidate must submit a programme of the proposed research. He is advised to submit an alternative scheme in case of difficulties about the first one.

9. It is advisable for the candidate to indicate at what institution he proposes to undertake the research and he should also state whether he is in a position to make any arrangements to carry out the research at the proposed institution.

10. The successful candidate must undertake to return to South Africa for a period of at least two years after the termination of the award.

11. The Selection Committee consists of:
Dr. H. Brown (*Cape Town*);
Prof. F. Forman (*Cape Town*);
Prof. I. Gordon (*Durban*);
Dr. A. Landau (*Cape Town*);
Dr. D. P. Marais (*Cape Town*);
Prof. S. F. Oosthuizen (*Pretoria*);
Mr. G. Sacks, F.R.C.S. (*Cape Town*);
Dr. G. Selzer (*Honorary Secretary, Cape Town*);
Dr. H. A. Shapiro (*Honorary Chairman, Johannesburg*).

12. Applications must be forwarded to:
Dr. H. A. Shapiro (*Honorary Chairman*),
Selection Committee, Eli Lilly Medical Research Fellowship (South Africa),
P.O. Box 1010, Johannesburg.

They must reach him not later than 1 May 1961.

They should be concise, and accompanied by the names of not more than two suitable referees. Testimonials must not be included.

SMITH, KLINE AND FRENCH LABORATORIES AWARD FOR POST-GRADUATE CLINICAL STUDY IN SOUTH AFRICA

1961 FELLOWSHIP

This award has been established by a grant from SKF Laboratories (Pty.) Limited, P.O. Box 784, Port Elizabeth. This is the South African branch of Smith, Kline and French Laboratories Ltd., London.

The Selection Committee (an entirely independent board of medical practitioners) consists of the following:
Prof. J. F. Brock (*Cape Town*);
Prof. E. H. Cluver (*Johannesburg*);
Prof. G. A. Elliott (*Johannesburg*);
Prof. J. H. Louw (*Cape Town*);
Dr. H. A. Shapiro (*Honorary Chairman, Johannesburg*);
Dr. M. Shapiro (*Johannesburg*);
Dr. M. M. Suzman (*Johannesburg*);
Prof. H. W. Snyman (*Pretoria*).

Applications are invited from registered *general practitioners* who have been in active practice in South Africa for at least 7 years.

The Bursary in intended for post-graduate clinical study and not for medical research. It is available for not less than a 2-month period at any Medical School in South Africa.

The total value of the Bursary is R600.

The candidate must submit a brief statement of his proposed course of study and indicate the institution at which he intends to undertake it.

No payments will be disbursed to the successful applicant until he has satisfied the Selection Committee that he has been accepted for the period of post-graduate study at a South African Medical School.

Applications must be made on the prescribed form which is obtainable from:
Dr. H. A. Shapiro (*Honorary Chairman*),
Selection Committee,
SKF Laboratories Award for Post-Graduate Clinical Study,
P.O. Box 1010, Johannesburg.

Closing Date for Applications: 30 June 1961.

* * *

JOHNSON & JOHNSON AWARDS FOR POST-GRADUATE CLINICAL STUDY IN SOUTH AFRICA

FOUR AVAILABLE FELLOWSHIPS FOR GENERAL PRACTITIONERS IN 1961

These Awards have been established by a grant from Johnson & Johnson (Pty.) Ltd., P.O. Box 727, East London.

The Selection Committee (an entirely independent board of medical practitioners) consists of the following:
Prof. S. F. Oosthuizen (Pretoria) *Chairman*;
Dr. P. F. H. Wagner (East London), *Vice-Chairman*;
Dr. H. A. Shapiro (Johannesburg) *Honorary Secretary*;
Dr. Beck de Villiers (Bloemfontein);
Dr. H. Grant-Whyte (Durban);
Prof. H. W. Snyman (Pretoria).

Applications are invited from registered *general practitioners* who have been in active practice in South Africa for at least 7 years.

The Bursary is intended for post-graduate clinical study and not for medical research. It is available for not less than a 2-month period at any Medical School in South Africa.

The total value of each Bursary is R600.

The candidate must submit a brief statement of his proposed course of study and indicate the institution at which he intends to undertake it.

No payments will be disbursed to the successful applicant until he has satisfied the Selection Committee that he has been accepted for the period of post-graduate study at a South African Medical School.

Applications must be made on the prescribed form which is obtainable from:

Dr. H. A. Shapiro (Honorary Secretary),
Selection Committee,
Johnson & Johnson Awards for Post-Graduate Clinical Study,
P.O. Box 1010, Johannesburg.

Four Fellowships will be available for Award during 1961.

Closing date for Applications: 1 August 1961.

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EXCERPTA CRIMINOLOGICA

The Excerpta Criminologica Foundation in co-operation with Excerpta Medica will start the publication of an abstracting service in the field of criminology under the title Excerpta Criminologica.

Publication schedule: Bimonthly—6 issues per year.

Language: English.

Contents: Abstracts of the world's literature in the field of criminology and related subjects.

Chief Editors: Prof. Th. Würtenberger, Freiburg/Br.; Prof. T. C. N. Gibbens, London; Prof. W. H. Nagel, Leyden.

Subscription price: R20 (£10) + postage 60c (6s.) per year.

This publication is of great importance to criminologists, criminological institutes, law schools, sociological and psychological institutes, psychiatrists, police authorities, prison administrators, welfare workers.

Write to:
Excerpta Criminologica Foundation,
119-123 Herengracht, Amsterdam,
The Netherlands.

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SABOURAUDIA: A NEW MYCOLOGICAL JOURNAL

E. & S. Livingstone Limited have published the first issue of a new journal which has been given the title *Sabouraudia*, as eponymous recognition of the great role played by Sabouraud in mycology.

The first issue includes the following original articles:

Yeasts from Human Sources (Mackenzie).

Pathogenicity of Candida Albicans and Candida Tropicalis (Hansenclever and Mitchell).

Moniliasis in Partridges (Keymer and Austwick).

Studies of the Invasive, Mycelial Form of Candida Albicans (Gresham and Whittle).

Reproduction and Pathogenicity of Cryptococcus Neoformans (Bergman).

Nannizzia Incurvata gen. nov., sp. nov., A Perfect State of Microsporum Gypseum (Bodin) Guiart et Grigorakis (Stockdale).

The Perfect States of Keratinomyces Ajelloi Vanbreuseghem Trichophyton Terrestre Durie & Frey and Miscrosporum Nanum Fuentes (Dawson and Gentles).

The Extra-Human Occurrence of Trichophyton Tonsurans var. Sulphureum in a Residential School (Mackenzie).

There is also topical news of interest to mycologists, including announcements of films, e.g. *The Griseofulvin Story* (Glaxo Laboratories Ltd.) and a *Study of Madura Foot* (Institut Pasteur).

There are four issues a year. The subscription is R8 (£4) per volume. Subscriptions should be sent in advance to the publishers:

E. & S. Livingstone Limited,
15–17 Teviot Place,
Edinburgh 1, Scotland.

REVIEWS OF BOOKS

MODERN TRENDS IN UROLOGY

Modern Trends in Urology: Second Series. Ed. by Sir Eric Riches, *M.C.*, M.S., F.R.C.S. (1960. Pp. 287 + Index. With 123 Figs. R 7.00 plus 25c postage).
London and Durban: Butterworth & Co. (Publishers) Ltd.

It was in 1953 that the first series of *Modern Trends in Urology* was published by Sir Eric Riches.

In few of the surgical specialities have advances been more rapid and striking than in urology. The second series of *Modern Trends in Urology*, published late in 1960, is therefore well timed, and it affords a completely new series compiled by an outstanding and distinguished team of contributors.

The first chapter written by G. A. Smart, Professor of Medicine at Durham University deals with *Metabolic Disorders in Renal Disease*. This branch of medicine plays an increasingly important role in the relationship of medicine to urinary disease.

The chapter on *Nephro-Calcinosis*, written by Prof. L. N. Pyrah, sets out the general considerations, the detailed approach and the handling of this most difficult subject. There are few, if any, more experienced than Professor Pyrah to discuss this problem.

The chapters on the *Artificial Kidney* and the *Image Intensifier* have now placed these important subjects in their correct perspective in modern urological practice.

Sir Eric Riches himself has written 3 important chapters, not the least of which is Chapter 19, in collaboration with Dr. B. W. Windeyer, and which relates the results of supervoltage therapy on carcinoma of the bladder, based largely on the extensive number of cases treated by them.

It is not possible, in so short a summary, to enumerate all the intriguing and absorbing urological problems which are discussed and described in this book; but the comprehensive survey of the use of small and large bowel in urological surgery, as well as the account given of hypertension due to renal artery disease, warrant special mention.

Altogether, *Modern Trends in Urology*, is an essential book of reference for urologists as well as all those who wish to advance their knowledge of this ever-expanding branch of surgical practice.

RESPIRATION: PHYSIOLOGY AND CLINICAL APPLICATIONS

Respiration: Physiologic Principles and their Clinical Applications. By P. H. Rossier, A. A. Buhlmann and K. Wiesinger. Ed. and translated by P. C. Luchsinger, M.D. and K. M. Moser, M.D. (1960. Pp. 494 + Index. With 95 Illustrations. R13.35).
St. Louis: The C. V. Mosby Company.

The Editors of the English edition of this book state in their preface that:

'The information gathered together in this volume should be made available in the English language to fulfil the need for a comprehensive text dealing with cardiopulmonary physiology and its clinical implications.'

This view can be endorsed. The fact that the editors were also the translators has led to a text singularly free of errors of language or syntax. The prose is fluent, readable and clear.

The book is divided into 4 parts, the first dealing with the normal physiology of respiration; the second with investigative methods in pulmonary function; the third with the pathophysiology of respiration; and the fourth with pulmonary insufficiency in clinical practice. Under these 4 headings almost every aspect of modern pulmonary physiology and its clinical significance is discussed and the relevant literature reviewed, from pressure in the pleural space to pulmonary function in pregnancy.

There are a number of relevant minor criticisms. There are rather few references more recent than 1958. No mention is made of Astrup's important contributions on pH and acid-base balance or of Astrand's work on exercise and physical fitness. The use of whole body plethysmography is dealt with in one paragraph, which does not include an explanation of the principles involved. Some of the diagrams are difficult to comprehend.

The bibliography is extensive up to 1958 and there are 80 pages of references. The references are grouped under subject headings which correspond roughly to similar headings in the text, but difficulty was encountered in trying to trace certain references quoted in the text. The European literature is mainly surveyed, a fact that adds to the value of the book for English-speaking readers, but major English and American contributions are nevertheless well represented.

The book may be recommended confidently to all those interested in or concerned with pulmonary physiology, normal and abnormal. It is very well produced, accurate and a mine of information.

UROLOGY IN GENERAL PRACTICE

Urology in General Practice. By Ian Parton, M.B., Ch.B., B.Sc. (N.Z.), F.R.C.S. (Eng.). (1960. Pp. 293 + Index. With 35 Figs. R 4.50 plus 30c. postage).
London and Durban: Butterworth & Co. (Publishers) Ltd.

This survey of modern urological practice has been specifically designed for the general practitioner. It is essentially a practical approach to the many everyday problems of the subject and is not intended to be a complete textbook of urology.

The chapters are well set out and well illustrated. They deal largely with methods and procedures employed daily in urological diagnosis and treatment. The author has taken great pains to ensure that each chapter deals with its subject matter lucidly and concisely; and considerable attention is paid to detail both in respect of diagnosis and of treatment. Not only are the more usual problems of urology, such as *Incontinence, Retention, Haematuria* and *Stone,* etc. carefully discussed; but the chapters relating to *Hermaphroditism, Problems in Paediatric Urology,* and the *Management of Bags and Drainage Catheters,* are also of inestimable value to the busy practitioner.

The last 2 chapters on *Recent Advances in Urology,* and *Emergency Operations* are of great interest and assistance, particularly to the practitioner who may be called upon to handle some of the emergencies that may arise.

Urology in General Practice should prove an interesting and accurate guide to the practice of urology.

PREPARATIONS AND APPLIANCES

CELESTONE (BETAMETHASONE) 0.5 MG.

SCHERING CORPORATION U.S.A.

Description: Celestone is betamethasone, a new synthesized derivative of prednisolone which possesses hormonal and metabolic effects common to all anti-inflammatory adrenocortical steroids but exhibits these effects in markedly different proportions. **Celestone** is available in tablets of 0.5 mg., scored for convenient fractional dosage.

Indications: **Celestone** is indicated in the management of various allergic, dermatologic, rheumatic, ocular and other conditions known to be responsive to corticosteroid therapy. **Celestone** is particularly recommended for patients who have shown a diminution in response to other anti-inflammatory corticosteroids and may be useful in those who have developed severe, incapacitating side effects on previous hormonal therapy.

Advantages: **Celestone** possesses certain advantages over older corticosteroids. It affords a greatly enhanced anti-inflammatory effect with the use of lower dosages, and certain undesirable side effects such as abnormal salt and water retention and excessive potassium excretion are not discernible in most patients receiving usual therapeutic dosages.

The glucocorticoid activity of **Celestone** is approximately 2 to 5 times that of prednisolone. Although sodium retention is characteristically associated with older corticosteroids, **Celestone** has been found in these same animal studies to produce an increase in sodium excretion.

No new side effects have been observed with **Celestone,** and steroid effects associated with certain other corticoids such as anorexia, protracted weight loss, vertigo, severe headache and muscle weakness do not appear to be characteristic of **Celestone.** However, **Celestone** is a potent corticosteroid and therefore is

capable of producing certain effects associated with adrenocortical therapy.

Dosage and Administration: The dosage of **Celestone** must be determined and adjusted to the individual requirements of the patient, i.e. severity of the condition, anticipated duration of therapy, tolerance to the steroid and response obtained. As with all corticosteroids, the lowest dose that will produce the desired clinical effect should be employed.

Packaging: **Celestone** Tablets 0.5 mg., bottles of 30's, 100's and 500's.

CIROTYL LIQUID LAXATIVE

AN IMPROVED FORMULA

The addition of a wetting agent and faecal softener to the formula of **Cirotyl** makes this liquid laxative doubly effective in that it combines several desirable features in one product.

Description: **Cirotyl** is a cherry-flavoured liquid **dual-action** laxative preparation containing as its active constituents diacetoxydiphenylisatin and propylene oxide ethylene oxide polymer.

Diacetoxydiphenylisatin is a synthetic form of the active principle of prunes; its gentle but persistent action mildly stimulates normal peristalsis.

The propylene oxide ethylene oxide polymer is a wetting agent and faecal softener, which acts as a surface tension depressant permitting fluids in the colon to penetrate into, and soften, hard, dry faecal matter. This results in a softer and more homogeneous stool which is then easily evacuated aided by the mild peristaltic action of diacetoxydiphenylisatin.

Cirotyl counteracts intestinal atonicity through a double mechanism; by direct chemical stimulus of the mucosa and by reflex stimulus through absorption and retention of fluids in the faeces.

Indications: **Cirotyl** is indicated for the prevention and treatment of occasional or habitual constipation and in cases where it is necessary to maintain the stools soft, as in pre- and post-surgical patients, in cases of anal fissure, rectal abscesses or haemorrhoids, during pregnancy and convalescence, in invalids, geriatric and sedentary patients or patients confined to bed for long periods, in paralysis or muscular weakness, and in patients with cardiovascular disease.

Dosage and Administration: The recommended initial dosage is as follows:

Infants, ¼ to ½ teaspoonful;
Children 1 *to* 6 *Years*, ½ to 1 teaspoonful;
Children above 6 *Years and Adolescents*, 1 teaspoonful;
Adults, 2 teaspoonfuls.

Water should be taken after each dose, which should be administered at bedtime or in the early morning before breakfast.

As the optimal dose varies from patient to patient according to the degree of constipation, the dosage schedule should be adjusted to fit each individual case.

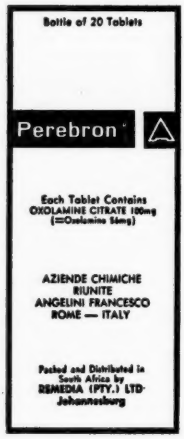
Package Information: **Cirotyl** is supplied in bottles of 4 fl. oz., each teaspoonful (5 ml.) of the suspension containing 2 mg. of diacetoxydiphenylisatin and 100 mg. of propylene oxide ethylene oxide polymer.

Manufactured by Parke Davis Laboratories (Pty) Ltd., Isando, Transvaal.

PEREBRON

(OXOLAMINE ANGELINI)

Perebron contains a new substance, Oxolamine, developed by the Research Laboratories of A.C.R.A.F. **Perebron** is a specific antitussive agent. It has anti-spasmodic and anti-inflammatory activity combined with analgesic action of the acetylsalicylic acid type.



Perebron does not merely suppress coughing, as expectoration tends to increase during the first 24-48 hours of medication, followed usually by marked diminution of secretion. During treatment with **Perebron** there is marked decrease in bronchospasm and inflammation and decrease in the discomfort usually associated with cough.

Indications: Acute and chronic cough, bronchitis, bronchial asthma, laryngotracheitis, pertussis, smoker's cough and complications of the common cold.

Presentation: Tablets each containing Oxolamine Citrate 100 mg. (= Oxolamine 56 mg .). Since **Perebron** is equally effective whether administered as a tablet or in a liquid vehicle, tablets are offered as giving greater accuracy of dosage and patient convenience.

Dose: Adults and children over 10 years—1-2 tablets 4-hourly. Children under 10 years—1 tablet 4-hourly.

Available in bottles of 20 tablets.

Packed and Distributed in the Union of South Africa by: Remedia (Pty.) Ltd., Johannesburg.

CORRESPONDENCE

HYPOTENSIVE ANAESTHESIA IN PATIENTS WITH CORONARY ARTERY DISEASE

To the Editor: I have read with great interest and I am deeply impressed by Dr. H. Bentel's paper on *Hypotension and Shock*, published in your journal on 30 July 1960. My colleagues join me in offering our congratulations on this excellent piece of work. I agree completely with Dr. Bentel on all points except his exclusion of patients with coronary disease. I have now used hypotension (with vasodilatation) for many of these cases, often as low as 50 or 60 mm. Hg systolic, with completely satisfactory results. I am convinced that a hypotensive method of anaesthesia is the method of choice for patients with 'bad' hearts.

I have no doubt that the prevention of vasoconstriction is the only rational approach to the prevention and treatment of shock of all kinds. This idea should be propagated as widely as possible.

Michael Johnstone, M.D.,
Consultant Anaesthetist.

Royal Infirmary,
Manchester.